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Award Number: W81XWH-05-1-0099

TITLE: SLEEP AND PERFORMANCE RESEARCH CENTER

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CONTRACTING ORGANIZATION:

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REPORT DATE: Tæ 2013

TYPE OF REPORT: Final Addendum

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

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# Form Approved REPORT DOCUMENTATION PAGE OMB No. 0704-0188 Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS. 1. REPORT DATE 2. REPORT TYPE 3. DATES COVERED May 2013 1 May 2012 - 30 April 13 Final Addendum 4. TÎTLE AND SUBTITLE 5a. CONTRACT NUMBER SLEEP AND PERFORMANCE RESEARCH CENTER **5b. GRANT NUMBER** W81XWH-05-1-0099 5c. PROGRAM ELEMENT NUMBER 6. AUTHOR(S) 5d. PROJECT NUMBER **5e. TASK NUMBER** Gregory Belenky, MD 5f. WORK UNIT NUMBER 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) 8. PERFORMING ORGANIZATION REPORT NUMBER Washington State University Spokane, WA 99202 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) 10. SPONSOR/MONITOR'S ACRONYM(S) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 11. SPONSOR/MONITOR'S REPORT NUMBER(S) 12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited 13. SUPPLEMENTARY NOTES 14. ABSTRACT The key deliverable in this award's statement of work is to "Develop a new program at Washington State University –the Spokane Sleep Research Initiative to focus on the effects of sleep and sleep loss on human performance." As the Spokane Sleep Research Initiative grew, it was renamed the Sleep and Performance Research Center (SPRC). Two major studies, one demonstrating in a laboratory study of human volunteers that split sleep sustains performance better than consolidated sleep if the consolidated sleep is during the day but worse than consolidated sleep if the consolidated sleep is in the night, and the other demonstrating in a field study that commercial bus drivers sleep adequate amounts on both off duty days, work a 40-50 hour work week and work on average a 10 hour work day where published during the interval covered by this final addendum (05/01/2012-04/30/2013). Other studies were published by SPRC core faculty during the same period concerned with the neurobiology of sleep, the behavioral consequences of sleep loss, and the use of mathematical models in fatigue risk management. During the interval covered by this final addendum (05/01/2012-04/30/2013) the Sleep and Performance Research Center 11 core faculty members produced 54 publications (see References) 15. SUBJECT TERMS- sleep, sleep loss, human performance 16. SECURITY CLASSIFICATION OF: 17. LIMITATION 18. NUMBER 19a. NAME OF RESPONSIBLE PERSON

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#### Introduction

The Sleep and Performance Research Center (SPRC) conducts human and animal studies in laboratory and field settings in support of basic and applied sleep research at Washington State University (WSU). The SPRC focuses on understanding the brain organization of sleep in humans and animals and on using this understanding to link sleep, by way of the underlying neurobiology, to key indicators of performance, be they physiological, behavioral or cognitive. The research contributes to sustaining human productivity, safety, health, and wellbeing and may contribute to the understanding of the neurobiology of consciousness.

The SPRC core faculty members are:

Gregory Belenky, M.D., Research Professor, VCAPP, WSU Spokane (SPRC Director)

Christopher Davis, Ph.D., Assistant Research Professor, WWAMI, WSU Spokane

Lois James, Ph.D., Assistant Research Professor, Criminal Justice and Criminology, WSU Spokane

Levente Kapás, M.D., Ph.D., Associate Professor, VCAPP, WWAMI, WSU Spokane

Ilia Karatsoreos, Ph.D., Assistant Professor, VCAPP, WSU Pullman

James Krueger, Ph.D., Regents Professor, VCAPP, WWAMI, WSU Spokane

Jaak Panksepp, Ph.D., Professor, VCAPP, WSU Pullman

David Rector, Ph.D., Professor, VCAPP, WSU Pullman (left WSU in 2011)

Éva Szentirmai, M.D., Ph.D., Assistant Professor, VCAPP, WWAMI, WSU Spokane

Hans Van Dongen, Ph.D., Research Professor, VCAPP, WSU Spokane (SPRC Assistant Director)

Bryan Vila, Ph.D., Professor, Criminal Justice and Criminology, WSU Spokane

Jonathan Wisor, Ph.D., Associate Professor, VCAPP, WWAMI, WSU Spokane

The current eleven SPRC core faculty members are all involved in sleep research and their productivity is evidenced by their collective publications and extramural funding. SPRC core faculty members are internationally renowned for their scientific contributions, which have led to paradigm shifts in science and policy changes at the state and national levels.

#### Program of Research

#### Field Studies in Humans

In a field study of commercial motor coach drivers (Belenky, Wu, Zaslona, and Hodges, 2012), we demonstrated that motor coach drivers worked long but not excessively long work days and work weeks, had duty start times that clustered in the morning, and slept reasonable amounts (7-9 hours) on on-duty and off duty days. They did not push regulatory limits. These data suggest that the majority of drivers live within reasonable limits when it comes to work and sleep. Further, the data suggest that fatigue risk mitigation should target outliers in terms of both drivers and companies relative to sleep, duty days, and start times.

In a field study of solo racing sailors (Hurdiel, et al., 2012), the relationship between amount of sleep and functional impairment in performance was assessed. Moderate to severe sleep restriction over multi-day races yielded technical errors, mood changes, and hallucinations.

In a field study of police officers (Violanti, et al., 2012), the relationship between shift work and injury was assessed. Higher injury risk was associated with night shift work.

# Laboratory Studies in Humans

In a laboratory study of sleep and performance in normal human volunteers (Belenky, Jackson, Tompkins, et al., 2012), we compared split sleep (sleep split into two or more periods) to consolidated nighttime sleep and consolidated nighttime sleep. We found that over a five-day simulated work-week volunteers splitting their sleep obtained more sleep than volunteers consolidating their sleep during the day and less sleep than volunteers consolidating their sleep during the night. These data suggest the value of more flexible rules governing sleeper berth use in motorcoach and trucking operations.

In a laboratory study over five nights of sleep restriction (Reynolds, et al., 2012), healthy, young men were measured for glucose metabolism, leptin, and testosterone. It was found that this short term sleep curtailment lead to changes in glucose metabolism and adrenal reactivity, which if experienced repeatedly might increase the risk for type 2 diabetes.

In a laboratory study in normal human volunteers (Van Dongen, Bender, and Dinges, 2012), it was found that systematic individual differences in the sleep homeostat and circadian rhythm modulated neurobehavioral impairment during sleep deprivation.

In a laboratory study in normal human volunteers (Van Dongen, 2012), it was found that trait vulnerability to neurobehavioral deficits in total sleep

deprivation predicted individual differences in cumulative impairment in response to multi-day sleep restriction.

#### Integrated Laboratory and Field Studies in Humans

A novel and ingenious study of working police officers (Waggoner, et al., 2012) simulated driving performance, tested psychomotor vigilance, and assessed subjective sleepiness and found these to be significantly degraded following 5 consecutive night shifts as compared to 3 consecutive days off duty, indicating that active-duty police officers are susceptible to performance degradation as a consequence of working nights.

#### **Laboratory Studies in Animals**

We conducted a number of laboratory animal studies including demonstrating a dose dependent effect of androgens on the circadian timing system (Butler, et al., 2012), measuring, using optogenetic methods, real-time lactate concentrations in the rodent cerebral cortex (Clegern, et al., 2012), demonstrating that microRNA inhibitors differentially alter sleep and EEG delta wave activity in rats (Davis, et al., 2012), demonstrating impaired wake-promoting mechanisms in ghrelin receptor deficient mice (Esposito, et al., 2012), demonstrating a phase relationship between suprachiasmatic molecular rhythms, cerebral cortex molecular rhythms, and behavioral rhythms in early runner and nocturnal mice (Jiang, et al., 2012), demonstrating that social defeat is associated with diminished levels of orexin in mesolimbic reward systems (Nocjar, et al., 2012), demonstrating that central administration of ghrelin induces wakefulness in mice (Szentirmai, 2012), demonstrating a brain-specific interleukin-1 receptor is active in sleep regulation (Taishi, et al., 2012), and demonstrating that a metabolic-transcriptional network links sleep and cellular energetics in the brain (Wisor, 2012).

#### Reviews

Banks, et al. (2012) reviewed the neuroscience of sleep and circadian rhythms. Clinton, Davis and Krueger (2012) reviewed the role of cytokines in host defense and sleep. Davis and Krueger (2012) reviewed sleep and cytokines. Jewett and Krueger (2012) reviewed sleep regulation by interleukin-1 and tumor necrosis factor. Karatsoreos (2012) reviewed the effect of circadian rhythm disruption on mental and physical health. Rector (2012) reviewed electrophysiological and vascular responses across the night of sleep. Szentirmai and Kapás (2012) reviewed the role of ghrelin in health and disease. Van Dongen and Belenky (2012) reviewed the role of mathematical models predicting performance from sleep wake history and circadian phase in the management of fatigue risk. Wisor (2012) reviewed the effect of sleep loss on hippocampal function.

# **Key Research Accomplishments**

- Published a field study of sleep and performance in motor coach drivers
- Published a field study of sleep and performance in solo racing sailors
- Published a field study of shiftwork and injury in police officers
- Published a laboratory study on the sleep and performance effects of split vs. consolidated sleep
- Published a laboratory study on the effects of sleep restriction on glucose metabolism, leptin, and adrenal reactivity
- Published a laboratory study of the systematic differences in the sleep homeostat and its interaction with the circadian rhythm
- Published a laboratory study of the relationship of trait variability in total sleep deprivation and chronic sleep restriction
- Published a hybrid field/laboratory study of performance of police officers coming off multiple days of night shift vs. coming off multiple days off duty
- Published a number of laboratory studies in animals investigating the underlying neurobiology of sleep
- Published a number of reviews of various aspects of developing areas of sleep research and fatigue risk management

# Reportable Outcomes

- Motor coach drivers work long hours but nevertheless get adequate amounts of sleep
- Solo race sailors suffer sleep loss and consequent performance impairment while racing
- Police officers working night shift are more likely to be injured
- Split sleep in normal humans can be preferable to consolidated sleep depending on the temporal placement of the consolidated sleep
- A few days of sleep restriction in normal humans can dysregulate glucose metabolism, leptin levels, and adrenal activity which if repeated at frequent intervals could increase the risk of type 2 diabetes

#### Conclusions

Sleep, sleep loss, and performance are active areas of research with progress being made through field studies of humans, laboratory studies of humans and animals, hybrid field and laboratory studies of humans, and scholarly review of the existing scientific literature.

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